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VINYL-COPPER DERIVATIVES—XI[1]

REACTIVITY OF Z-ALKENYL CUPRATES TOWARDS VARIOUS ELECTROPHILES. APPLICATION TO THE SYNTHESIS OF SOME NATURAL PRODUCTS

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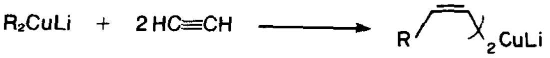
Abstract—*Z*-Alkenylcuprates **1** and **2**, prepared *in situ* by addition of acetylene to alkylcuprates, react with a variety of electrophiles (epoxides, carbon dioxide, aldehydes) and give conjugate addition products with α,β-unsaturated aldehydes, ketones and esters, and with activated cyclopropanes. They also add across the triple bond of some alkynes. The synthesis of natural products (**7**, **9**, **22**) is described.

In a previous communication[2] we reported the syn-addition of various cuprates to acetylene:

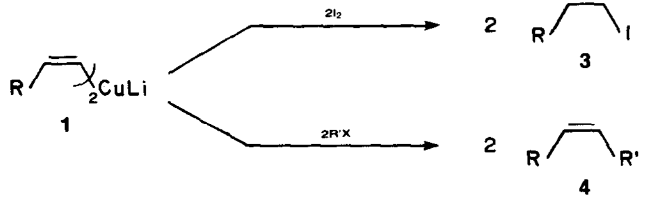


1

2a,b,c

(**2a**: $Z = OtBu$, **2b**: $Z = SPh$, **2c**: $Z = C{\equiv}C{-}nBu$)

The *Z*-alkenyl cuprates **1** and **2**, thus obtained, have been iodinated[1,2a] and alkylated[1] to afford stereospecifically and in high yield the iodides **3** or the olefin **4**:



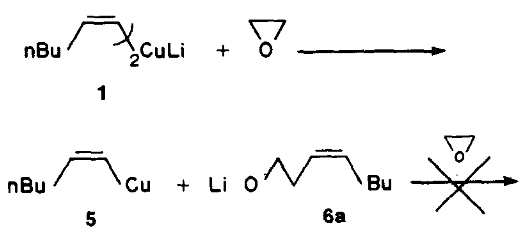
70–90%
$Z/E > 99.97\%$

70–95%
$Z/E > 99.95\%$

We describe herein, the reaction of these cuprates with a variety of other electrophiles. Moreover, we sought, as much as possible, for conditions where *both* *Z*-alkenyl groups of **1** were transferred, as was the case in the alkylation reaction.

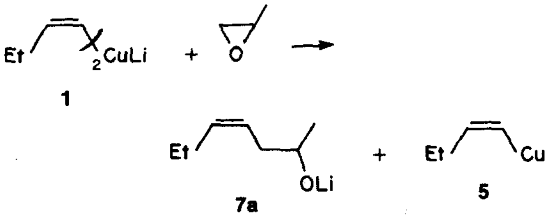
Reaction with epoxides

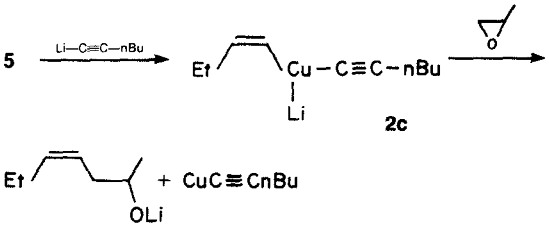
Organocuprates are known to react smoothly with epoxides,[3,4] although they are commonly used in large excess. Upon addition of 2 eq ethylene oxide to an ethereal solution of cuprate **1** (R=nBu) a 56% yield of homoallylic alcohol **6** was obtained after hydrolysis. This result indicates that the first *Z*-alkenyl group of **1** reacted very rapidly with the epoxide, whereas the anticipated heterocuprate (**5** + **6a**) reacted very sluggishly with the second equivalent of epoxide.



Warming the reaction mixture did not improve the yield and promoted coupling of vinyl-copper **5** (R=nBu) into *Z*,*Z*-5,7-dodecadiene.[3]

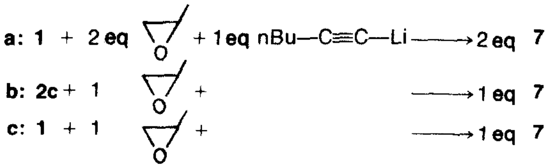
Since cuprates **2c** are prone to transfer only the *Z*-alkenyl group when reacted with epoxides,[4b] we anticipated that it would be possible to prepare such a species *in situ*. Thus, after the addition of two eq propylene oxide to cuprate **1** (R=Et), one eq Li–C≡C–nBu was immediately added:





7a

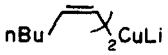
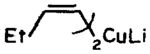
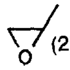
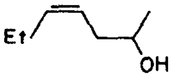
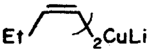
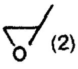
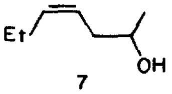
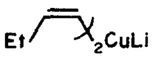
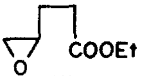
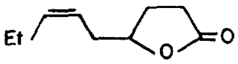
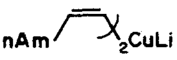
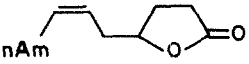
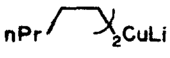
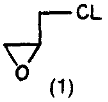
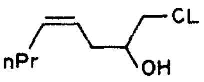
Cuprate **2c** (R=Et) formed in the reaction mixture reacted rapidly with the second eq of propylene oxide. The 82% yield of alcohol **7**, thus obtained, indicates that, in this procedure, *both* *Z*-alkenyl groups are transferred from only one copper(I) equivalent. Direct use of cuprate **2c** requires twice as much copper(I) salt. The choice between the three procedures:



depends on the respective availabilities of the R group in the cuprate, and of the epoxide (the use of heterocuprates **2a** and **2b** is not suitable, since they transfer also the hetero group to some extent): for example with the cheap propylene oxide, procedure (a) transfers the whole vinyl synthon (Table 1 entry 3) whereas a more sophisticated epoxide can be treated more simply according to procedures (b) or (c) (Table 1, entries 4 and 5).

The reaction of *Z*-dialkenyl cuprates **1** with propylene oxide proceeds only by attack on the less hindered side

Table 1. Reaction of cuprates **1** with epoxides

Entry	Cuprate **1**	Epoxide (equivalents)	Reaction conditions[a]	Product	Yield isolated[b]
1		 (2)	−30° to +15° 4 h	 **6**	56%
2		 (2)	−30° to +15° 4 h	 **7**	50%
3		 (2)	add. of LiC≡C—Bu −30° to −15° 2 h	 **7**	82%
4		 (1)	−30° to −10°	 **8**	82%
5		 (1)	−30° to −10° 2 h	 **9**	88%
6		 (1)	−30° to −25° 1 h	 **10**	96%

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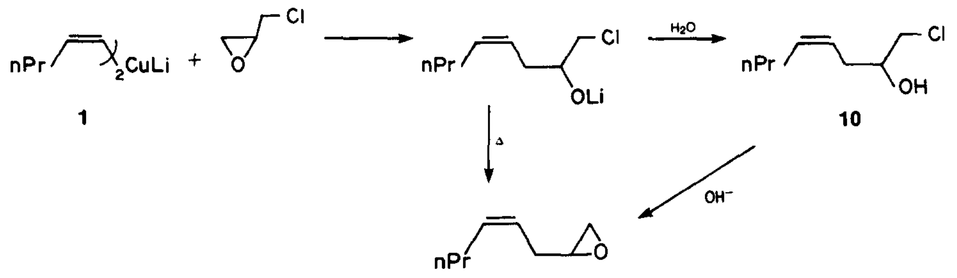
[a] All reactions are performed in Et_2O.

[b] Based on the epoxide consumed.

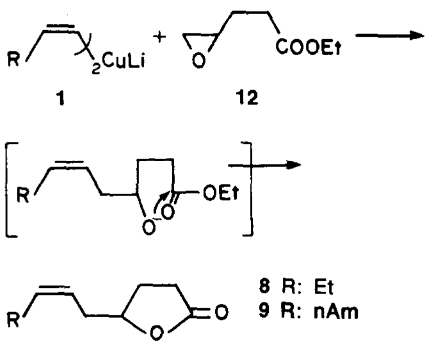
of the epoxide, as it is usually the case for cuprate reagents.[3]

Epichlorhydrin reacts readily with cuprates **1** (R=nPr) to afford the chlorhydrin **10** in excellent yield (Table 1, entry 6) provided that the temperature is maintained low enough to avoid the formation of the epoxide **11**.



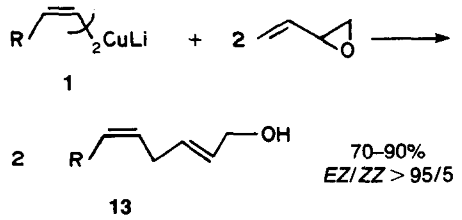
The opening of epoxides by cuprates **1** offers a new route to some natural products. Thus we have prepared the alcohol **7** (82% yield, 99.95% purity), which is the main component of the banana aroma.[5] Its previous synthesis from *Z*-alkenyl diethyl alane and propylene oxide[6] affords 53% yield of alcohol **7** of 65% purity.

Another class of natural products can be prepared by reacting cuprates **1** with epoxy-ester **12** (Table 1, entries 4 and 5) taking advantage of the non-reactivity of cuprates towards esters[7–9]



Lactone **9** has been found in cooked lamb,[10] butterfat,[11,12] the flower Polianthes tuberosa,[13] the pedal gland of the bontebok Damaliscus dorcas dorcas,[14] the cultured broth of *Sporobolomyces odorus*,[15] and the male tarsal scent of the black-tailed deer *Odocoileus hemionus columbianus*.[16] Many syntheses of this lactone have been reported[14,17] but this one is more straightforward, gives higher yield, and better *Z* isomeric purity (99.95%).

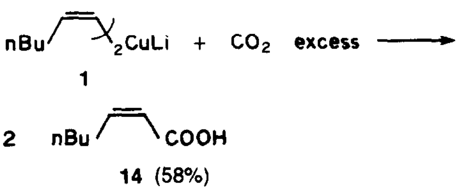
Finally, we have recently reacted cuprates **1** with α,β-unsaturated epoxides,[18] a case where *both* *Z*-alkenyl groups are transferred:



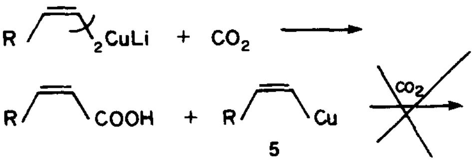
We have also used the *E,Z*-dienol **13** (R=Am) in the synthesis of the sex pheromone of the potato tuberworm moth *Phtorimaea operculella*.[19]

Reaction with carbonyl derivatives

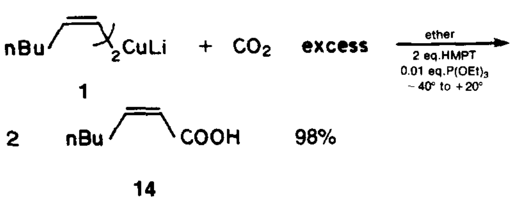
The reaction of organocuprates with carbon dioxide (CO_2) has not yet been reported to our knowledge. The only carbonations reported have been performed with organocopper reagents.[20–23] When a stream of CO_2 gas is passed on an ethereal solution of *Z*-dialkenyl cuprate **1** (R=nBu) an exothermic reaction is observed, and the *Z*-alkenoic acid **14** is obtained after hydrolysis:



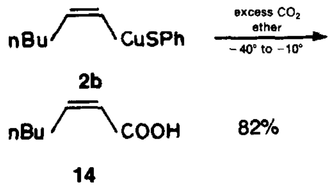
The 58% yield (based on *both* *Z*-alkenyl groups) indicates that, here again, the first *Z*-alkenyl group reacted rapidly whereas the vinyl-copper reagent **5** reacted very sluggishly with CO_2:



Therefore, *in situ* reaction conditions necessary for the carbonation[21] of **5** were applied; 2 eq HMPT and 0.01 eq of $P(OEt)_3$ (as catalyst) were added to cuprate **1** (R=nBu) and after carbonation we obtained an excellent yield of acid **14** (the normal reaction conditions for an organocopper reagent associated with a magnesium salt.[21] The normal reaction conditions for an organocopper reagent associated with lithium salts, as vinyl-copper **5**, were 4 eq of TMEDA and 0.01 eq of $P(OEt)_3$, but under these conditions we only obtained a 61% yield of acid **14**).

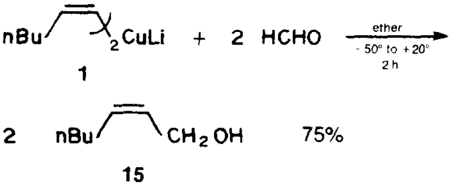


Cuprates **2**, also react readily with CO_2, *without* the addition of HMPT. For example:



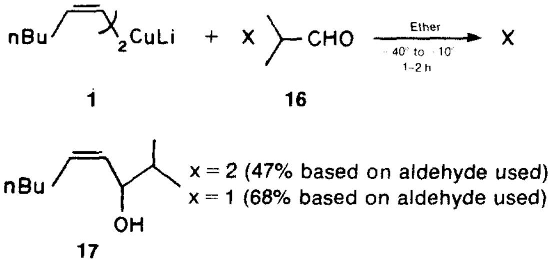
The stereochemical purity of this acid has been found superior to 99.94% *Z* by capillary gas chromatography and by ^{13}C NMR. Thus, the method appears to be the best available for the preparation of *Z*-alkenoic acids such as **14**.

The reaction of cuprate reagents with aldehydes has not received much attention since cuprates are usually prepared from the corresponding organolithium or organomagnesium derivatives. Aldehydes are known to react with organocopper[24] or cuprate[25] reagents, although there is no example in the literature of reaction with alkenyl–copper or cuprate derivatives. Upon introduction of a stream of formaldehyde gas into an ethereal solution of cuprate **1** (R=nBu), the product obtained, after hydrolysis, was the expected allylic alcohol of *Z*-configuration, **15**:

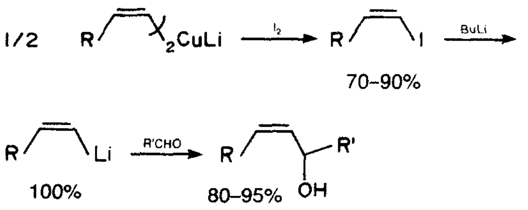


Thus, in this case, *both Z*-alkenyl groups of **1** reacted. The vinly–copper **5** which is formed during the reaction reacts with the extremely reactive formaldehyde. Again, the *Z*-purity of the alcohol **15** is greater than 99.96% and this reaction constitutes a general entry to *Z*-allylic alcohols of very high purity.

The reaction with less reactive aldehydes such as isobutyraldehyde **16** gives less satisfactory results, since only one *Z*-alkenyl group of cuprate **1** reacts:



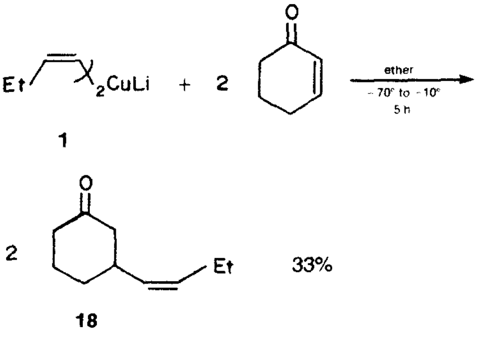
To obtain alcohols such as **17** it seems preferable to proceed in two steps, via the corresponding *Z*-iodoalkene[2]



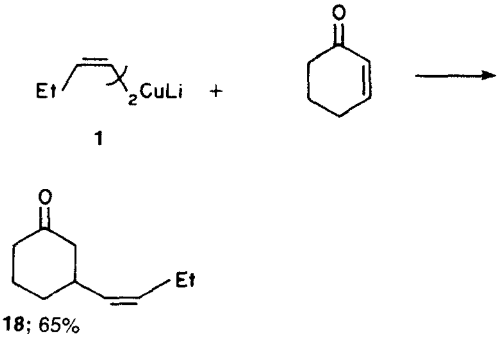
which is transformed into its lithium derivative by lithium–halogen exchange.[26] In this reaction sequence *both Z*-alkenyl groups are used and the overall yield is also much better.

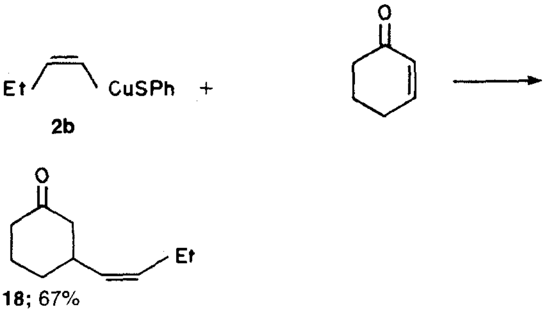
Conjugate addition reactions

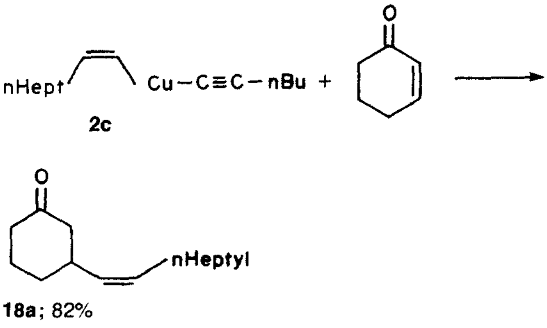
The most popular reaction of organocopper and -cuprate reagents is conjugate addition to α,β-unsaturated compounds.[7,22,27,28] Alkenyl-cuprates have also been extensively used in such reactions,[22,29–31] including prostaglandin syntheses.[32] The reaction of cuprates **1** (R=Et) with two eq cyclohexenone afforded the conjugate adduct **18** in disappointingly low yield:



Thus, it appears that the vinyl–copper **5** is unreactive towards enones (see however Ref. 31 for a reaction with a large excess of Me$_2$S). The use of stoechiometric amounts (1:1) of the reactants gives a better yield, depending on the type of cuprate used:

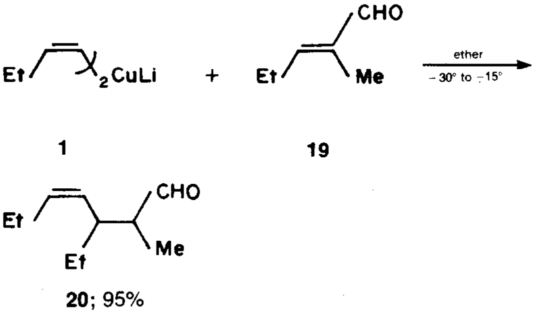






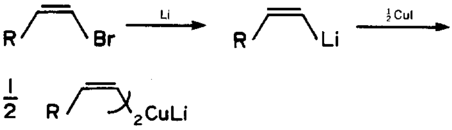
The best results are achieved with cuprate **2c** indicating that it is possible to obtain high yields of conjugate adduct without using an excess of cuprate reagent as is usually the case. Unsymmetrical cuprates R–Cu–C≡C–R′ have already been shown to be superior to the symmetrical ones (R_2CuLi) for conjugate addition.[33]

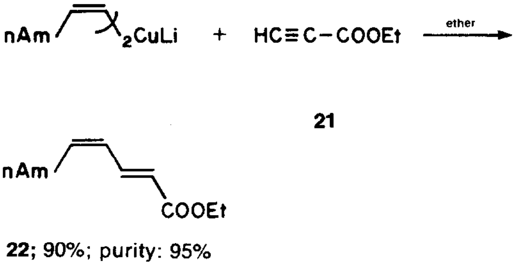
The reaction of cuprate **1** (R=Et) with α,β-unsaturated aldehydes also affords the conjugate adduct. For example (**1** + **19** → **20**):



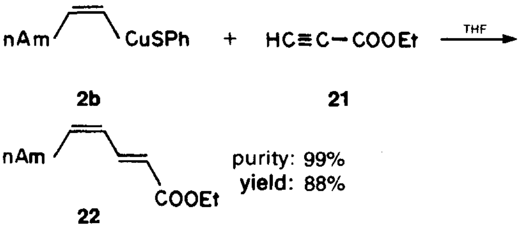
Using only one equivalent of aldehyde **19** an excellent yield of adduct **20** is obtained. Here, again, we were unable to transfer the second *Z*-alkenyl group of cuprate **1** (49% yield when 2 eq aldehyde are added). However, this conjugate addition of *vinylic* cuprates to α,β-unsaturated aldehydes is unprecedented and may be applied to other aldehydes of this type.[34] Only a few examples of 1–4 addition of alkyl cuprates to such aldehydes have been reported.[7,35]

The reaction of cuprates **1** with ethyl propiolate **21**, known to react with dialkyl cuprates[7,22,27,36] and also with alkenyl cuprates[29,30,37,39] with transfer of both alkyl groups,[40] has been studied. The reaction of cuprate **1** (R = nAm), prepared via its vinyl-lithium precursor, with ethyl propiolate **21** has been previously performed (using one eq of **21**) for the synthesis of Pear Ester **22**:[29]

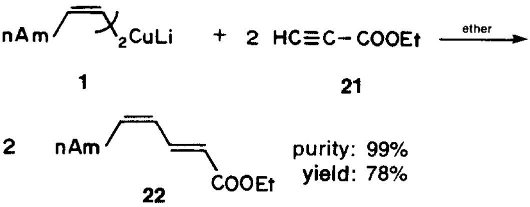




Since the preparation of the vinyl–lithium reagent from the corresponding *Z*-alkenyl bromide is *not stereospecific* (2–4% isomerisation[41]) it may be expected that the use of *stereospecific* *Z*-alkenyl cuprates **1** and **2** will afford pure Pear Ester. Actually, use of cuprate **2b** (R = nAm) affords Pear Ester in high yield and with an excellent stereochemistry:

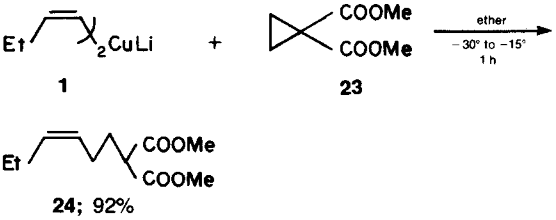


More interestingly, the reaction of cuprate **1** with 2 *eq* of ethyl propiolate **21** afforded the Pear Ester **22** in 78% yield with an excellent purity also (> 99%)



Thus, *both* *Z*-alkenyl groups of **1** are used and the method constitutes a general entry to conjugated *E,Z*-dienic esters.

Finally, cuprates **1** react also with activated cyclopropanes such as **23**:[42]



to afford the product **24** via the cyclopropane ring opening. In this case only one *Z*-alkenyl group of **1** is transferred whatever the reaction conditions tried.

Addition reaction to alkynes

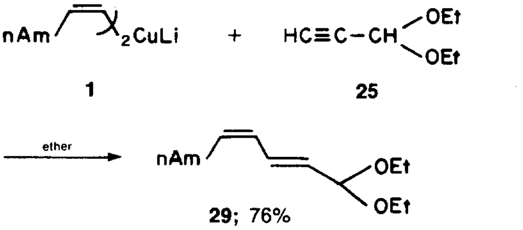
It has recently been shown that lithium dialkyl cuprates are able to add across the triple bond of some functionalized alkynes[38,39,43] such as:

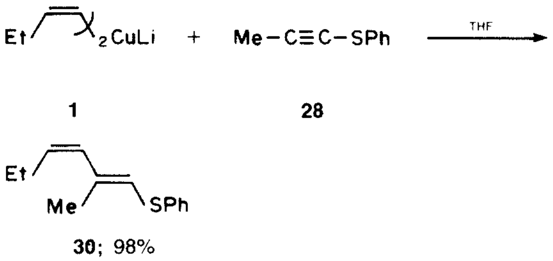
$HC{=}C{-}CH(OEt)_2$ **25**; $HC{\equiv}C{-}OEt$ **26**;

$HC{\equiv}C{-}SEt$ **27**; and $Me{-}C{\equiv}C{-}SPh$ **28**

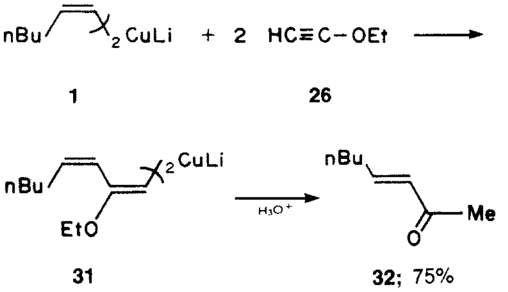
affording a vinyl–cuprate. In the case of **25**, **26** and **27** *both* alkyl groups of the cuprate are transferred.[44] We have studied the ability of vinyl cuprates **1** to add to these alkynes (vinyl cuprates are generally much less reactive than alkyl cuprates).

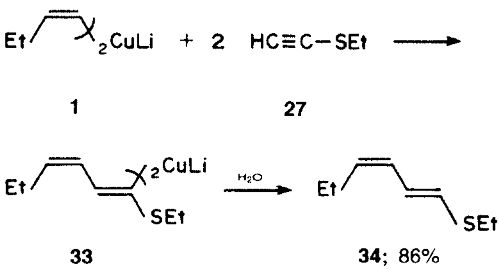
In the cases of alkynes **25** and **28** only one *Z*-alkenyl group is transferred affording the addition product in high yield





In the cases of alkynes **26** and **27** *both* *Z*-alkenyl groups are transferred and the new cuprates **31** and **33** are obtained before hydrolysis:





The acidic hydrolysis of cuprate **31** affords the intermediate *Z* ethylenic ketone which isomerizes rapidly to the trans one **32**. On the other hand cuprate **33** affords the dienic thioether **34** of pure *Z–E* configuration.

Cuprate **31** may be considered as a regiospecified enolate of the corresponding ketone **35**

whereas cuprate **33** is equivalent to the acyl carbanion **36**:

We are presently studying the synthetic potential of new cuprates **31** and **33**.

CONCLUSION

The addition of alkyl cuprates to acetylene which affords, quantitatively, the *Z*-alkenyl cuprates **1** and **2** may be considered, at present, the best way for the introduction of an ethylenic linkage of pure *Z*-configuration (>99.95%). The alternative preparation of these vinylic cuprates, starting from the pure vinylic halides (usually the bromide or the chloride), via the vinyllithium derivative, is not stereospecific.

The wide scope of reactivity of *Z*-alkenyl cuprates towards various electrophiles, combined with their functional selectivity, allows the synthesis of many natural products in high yield by a one-pot procedure.

EXPERIMENTAL

^{1}H NMR spectra were recorded on a Jeol MH 100 (CCl_4; δ ppm from TMS), ^{13}C NMR on a Jeol FX 60 Q ($CDCl_3$; δ ppm from TMS). IR spectra were obtained on a Perkin–Elmer model 457 spectrometer. GLC analyses were performed on a Carlo Erba gas chromatograph model G 1 and 2150 using a 3 m glass column (10% SE 30 or 10% LAC 860 on silanized chromosorb G 80/100 mesh) and a 50 m capillary glass column (OV 101). The gas chromatograph was coupled with an integrator LTT 9400. All reactions are performed under a nitrogen atmosphere in a 250 ml flask equipped with a low-temperature thermometer, a mechanical stirrer and a pressure equalizing addition funnel. The cuprates **1** and **2** are prepared as previously described.[2b,2c] Acetylene (1.32 l) was bubbled into a stirred ethereal solution of alkylcuprate (25 mmol for R_2CuLi, 50 mmol for R CuLi) at −60°C. After 30 min at −25°C the greenish solution of cuprates **1** or **2** was ready for use.

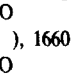
Reaction of Z-*alkenylcuprates with epoxides*

(Z)-3-*Octen*-1-*ol* **6**. To a stirred solution of cuprate **1** (R = nBu) (25 mmol) in 120 ml Et_2O, was added ethylene oxide (2.2 g, 50 mmol) at −30°. The reaction mixture was slowly warmed (2 h) to +15°, maintained 2 hr at this temperature, then hydrolysed at −10° with a mixture of 50 ml of saturated NH_4Cl solution and 50 ml 10% HCl. Hexane (100 ml) was added, then the mixture was filtered and decanted. The organic layer was washed successively with NH_4OH (5% solution; 50 ml) then 50 ml saturated NH_4Cl and dried over $MgSO_4$. The solvents were evaporated and the residue was distilled through a 10 cm Vigreux column to afford 3.58 g (56%) of product, b.p. 95–96°/15 mmHg (lit.[45] b.p. 96°/25 mmHg). n_D^{20} 1.4482 (lit.[45] n_D^{25} 1.4450). IR (neat) cm^{-1} 3350 (OH), 1660 (H-C=C-H): NMR (CCl_4, δ) 5.55 (CH=CH,m,2), 3.62 (CH_2-O,t,2), 2.32 (CH_2-CH_2-OH,q,2), 2.11 (CH_2-C=,q,2). Calc for $C_8H_{16}O$: C, 74.94; H, 12.57; found: C, 74.72; H, 12.72%.

(Z)-4-*Hepten*-2-*ol* **7**. Procedure as above with cuprate **1** (R = Et) (25 mmol) and propylene oxide (50 mmol) gave 2.85 g (50%), b.p. 61–62°/15 mmHg (lit[6] 58°–59°/10 mmHg). n_D^{20} 1.4498. IR (neat) cm^{-1} 3350 (OH), 1660 (H-C=C-H); ^{1}H NMR (CCl_4, δ) 5.35 (CH=CH,m,2), 3.73 (CH-O,m,1), 2.05–2.20 (CH_2-C=C-CH_2,m,4), 1.14 (CH_3-CH-O,d,3); ^{13}C NMR ($CDCl_3$, δ) 134.4, 125.2 (CH=CH), 67.8 (CH-O), 37.1, 22.7, 20.8 (CH_2), 14.3 (CH_3). Calc for $C_7H_{14}O$: C, 73.63; H, 12.35; found: C, 73.49; H, 12.49%.

Alternatively the same product may be prepared as follows: to the stirred solution of cuprate **1** (R = Et) (25 mmol) in 100 ml Et_2O was added propylene oxide (2.9 g, 50 mmol) at −30° and immediately after, a suspension of Li-C≡C-Bu) (25 mmol) (prepared by addition of BuLi to 1-hexyne in ether at 0°) in 60 ml Et_2O. The mixture is warmed to −15° and kept 2 hr at this temperature, then hydrolysed and worked-up as above. Yield 4.67 g (82%).

5-[(Z)-2-*Pentenyl*]*dihydro*-2-*furanone* **8**. To a stirred solution of cuprate **1** (R = Et) in 120 ml Et_2O, at −30°, is added 3.6 g (25 mmol) of epoxide **12** (prepared in 87% yield by reacting ethyl penten-4-oate with MCPBA in CH_2Cl_2). The mixture was allowed to warm to −10° in 1 hr, stirred one more hour and then hydrolysed with a mixture of 50 ml sat NH_4Cl and 20 ml 10% HCl. After addition of 150 ml hexane, the mixture was filtered and decanted, the organic layer was washed once with 50 ml 2% NH_4OH solution, then once with a mixture of 30 ml sat NH_4Cl and 10 ml 10% HCl and finally dried over $MgSO_4$. The solvents are evaporated and the residue is distilled through a 10 cm Vigreux column to afford 3.16 g (82%) of pure **8** b.p. 136–

138°/15 mmHg. n_D^{20} 1.4720. IR (neat) cm^{-1} 3010 (CH=CH), 1780 (- $C\begin{smallmatrix}/\!\!/O\\ \backslash O\end{smallmatrix}$), 1660 (H-C=C-H); NMR (CCl_4, δ) 5.49 (CH=CH,m,2), 4.52 (CH-O,m,1). Calc for $C_9H_{14}O_2$: C, 70.09; H, 9.15; found: C, 69.86; H, 9.28%.

5-[(Z)-2-*Octenyl*]*dihydro-2-furanone* **9**. Procedure as above (compound **8**), with cuprate **1** (R = nAm) (25 mmol) and epoxide **12** (25 mmol) gave 4.31 g (88%), b.p. 94–96°/0.05mmHg (lit[17b] 110–120°/0.05 mmHg); n_D^{20} 1.4692 (lit.[17b] n_D^{22} 1.4667, lit.[17c] n_D^{23} 1.4630); IR (neat) cm^{-1} 3010 (CH=CH), 1780 (lactone C=O), 1660 (H-C=C-H); ^{1}H NMR (CCl_4, δ) 5.51 (CH=CH,m,2), 4.49 (CH-O,m,1), 2.05–2.22 (CH_2,m,8), 1.30–1.35 (CH_2,m,6), 0.92 (CH_3,t,3); ^{13}C NMR ($CDCl_3$, δ) 177.5 (C=O), 134.4, 122.6 (HC=CH), 80.4 (CH-O), 33.0, 31.5, 29.2, 28.8, 27.5, 27.2, 22.6 (CH_2), 14.0 (CH_3). Calc for $C_{12}H_{20}O_2$: C, 73.42; H, 10.26; found: C, 73.35; H, 10.39%.

(Z)-1-*Chloro-4-Octen-2-ol* **10**. 4.62 g (50 mmol) of epichlorhydrin were added to a stirred soln of cuprate **1** (R = nPr) (50 mmol) in 180 ml Et_2O at – 30°. The mixture was kept at – 25° 1 hr, then hydrolysed with 100 ml sat NH_4Cl. After the addition of 150 ml hexane and filtration, the organic layer was washed once with 50 ml of 2% NH_4OH, then once with a mixture of 50 ml NH_4Cl sat. solution and 20 ml 10% HCl and finally dried over $MgSO_4$. Distillation affords 7.8 g (96%) or pure **10**, b.p. 54–55%/0.1 mmHg; n_D^{20} 1.4732; IR (neat) cm^{-1} 3400 (-OH), 3010, 1660 (H-C=C-H); NMR (CCl_4, δ) 5.42 (CH=CH,m,2), 3.78 (CH-O,m,1), 3.50 (CH_2-Cl,d,2), 2.32 (CH_2-C=,t,2), 2.04 (CH_2-C=,q,2), 1.41 (CH_2,m,2), 0.97 (CH_3,t,3). Calc for $C_8H_{15}OCl$: C, 59.07; H, 9.29; found: C, 59.21; H, 9.42%.

(Z)-2-*Heptenoic acid* **14**. 40 ml of THF were added to a stirred solution of cuprate **2b** (R = nBu) (25 mmol) in 100 ml Et_2O at – 40°. A stream of CO_2 (obtained by evaporation of dry ice) was bubbled into the reaction flask while the mixture is allowed to warm to – 10°. After 10 min, 80 ml of 10% HCl are added, then 100 ml of hexane. The precipate was filtered off, and the organic layer was washed once again with 50 ml 10% HCl. The acid **14** was extracted by washing the organic layer twice with 50 ml Na_2CO_3 and the aqueous phase acidified with 10% HCl and extracted with ether. The ether extracts were dried over $MgSO_4$. Distillation afforded 2.62 g (82%) of pure acid **14**, b.p. 72°/0.01 mmHg (lit.[46] b.p. 117°/16 mmHg); n_D^{20} 1.4542 (lit.[46] n_D^{22} 1.4449); IR (neat) cm^{-1} 1700 (COOH), 1645, 825 (H-C=C-H); ^{1}H NMR (CCl_4, δ) 6.39 (CH=,dt,1), 5.82 (CH=,d,1) (JH-=-H: 12 Hz), 2.72 (CH_2-C=,q,2); ^{13}C NMR ($CDCl_3$, δ) 173.1 (COOH), 153.7, 119.8 (HC=CH), 31.5, 29.2, 22.6 (CH_2), 13.9 (CH_3). Calc for $C_7H_{12}O_2$: C, 65.59; H, 9.43; found: C, 65.32; H, 9.67%.

Alternatively, acid **14** may be prepared as follows: to a stirred ethereal solution (100 ml) of cuprate **1** (R = nBu) (25 mmol) was added at – 40° 20 ml HMPT and 40 mg $P(OEt)_3$. A stream of CO_2 gas was bubbled into the solution and the temperature allowed to rise to + 20° (15 min), stirred for a further 2 hr, hydrolysed, and worked up as above. Yield: 6.27 g (98%).

(Z)-2-*Hepten*-1-*ol* **15**. A stream of gaseous formaldehyde (obtained by thermal depolymerisation of 3 g trioxymethylene) was bubbled into an ethereal solution (120 ml) of cuprate **1** (R = nBu) (25 mmol) at – 50°. The mixture was allowed to warm to room temperature (1 hr) stirred one more hour, then hydrolysed at – 10° with a mixture of 50 ml sat NH_4Cl and 30 ml 20% HCl. 100 ml of hexane were added and, after filtration, the organic layer was washed once with 50 ml 5% NH_4OH solution and once with 50 ml sat NH_4Cl then dried over $MgSO_4$. Distillation afforded 4.3 g (75%) of alcohol **15**, b.p. 78°/14 mmHg (lit.[47] b.p. 59.8–60°/4 mmHg); n_D^{20} 1.4473 (lit.[47] n_D^{20} 1.4430); IR (neat) cm^{-1} 3350 (-OH), 3010, 1660 (H-C=C-H); NMR (CCl_4, δ) 5.21 (CH=CH,m,2), 3.89 (CH_2-O,d,2), 1.97 (CH_2-C=,q,2). Calc for $C_7H_{14}O$: C, 73.63; H, 12.35; found: C, 73.48; H, 12.47%.

(Z)-2-*Methyl-4-nonen*-3-*ol* **17**. To a stirred solution of cuprate **1** (R = nBu) (50 mmol) in 180 ml Et_2O at – 40°, was added 3.6 g (50 mmol) of isobutyraldehyde. The reaction mixture was warmed to – 10° and after 15 min hydrolysed and worked up as for compound **15**. Distillation afforded 5.3 g (68%), b.p. 64–65°/0.1 mmHg; n_D^{20} 1.4490; IR (neat) cm^{-1} 3350 (-OH), 3010, 1660 (H-C=C-H): NMR (CCl_4, δ) 5.34 (CH=CH,m,2), 4.00 (CH-O,t,1), 2.06 (CH_2-C=,q,2). Calc for $C_{10}H_{20}O$: C, 76.86; H, 12.90; found: C, 76.72; H, 12.98%.

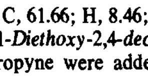
3-[(Z)-1-*Butenyl*]*cyclohexanone* **18**. To an ethereal solution (100 ml) of cuprate **1** or **2b** (R = Et) (25 mmol) at – 70° were added 2.4 g (25 mmol) of cyclohexenone. The mixture was allowed to warm to – 10° (1 hr) and after 10 min hydrolysed with 80 ml sat NH_4Cl 100 ml of hexane were added, the precipitate filtered off and the organic layer dried over $MgSO_4$. Distillation affords 2.47–2.55 g (65–67%) of pure ketone **18**; b.p. 102–103°/14 mmHg; n_D^{20} 1.4758; IR (neat) cm^{-1} 3005 (H-C=C-H), 1720 (C=O), 735 (H-C=C-H); NMR (CCl_4, δ) 5.30 (CH=CH,m,2). Calc for $C_{10}H_{16}O$: C, 78.89; H, 10.59; found: C, 78.72; H, 10.64%.

3-[(Z)-1-*Nonenyl*]*cyclohexanone* **18a**. Procedure as above with cuprate **2c** (R = nHeptyl) (25 mmol) and cyclohexanone (25 mmol) yielded 4.55 g (82%); b.p. 99–100°/0.05 mmHg; n_D^{20} 1.4688; IR (neat) cm^{-1} 3005 (H-C=C-H), 1720 (C=O); NMR (CCl_4, δ) 5.32 (CH=CH,m,2). Calc for $C_{15}H_{26}O$: C, 81.02; H, 11.78; found: C, 80.87; H, 11.92%.

(Z)-2-*Methyl-3-ethyl-4-heptenal* **20**. 4.9 g (50 mmol) of 2-methyl-2-pentenal **19** were added to a stirred solution of cuprate **1** (R = Et) (50 mmol) in 180 ml Et_2O at – 30°. The mixture was warmed to – 15° (15 min) and hydrolysed with 100 ml sat NH_4Cl. 150 ml of hexane were added and, after filtration, the organic layer was washed once with 100 ml NH_4Cl sat. solution and dried over $MgSO_4$. Distillation afforded 7.32 g (95%) of pure aldehyde **20**; b.p. 41°/0.01 mmHg; n_D^{20} 1.4457; IR (neat) cm^{-1} 2700, 1730 (CH=O), 1660, 735 (H-C=C-H); NMR (CCl_4, δ) 9.72 (-CHO,d,1), 5.60 (-CH=,dt,1), 5.21 (-CH=,dd,1) (JH-C=C-H: 11 Hz). Calc for $C_{10}H_{18}O$: C, 77.86; H, 11.76; found: C, 77.77; H, 11.89%.

(E,Z)-*Ethyl-2,4-decadienoate* **22**. To a stirred solution of cuprate **2b** (R = nAm) (25 mmol) in 100 ml Et_2O were added 40 ml THF at – 50° and then 2.45 g (25 mmol) of ethyl propiolate **21**. The mixture was warmed to – 20° and hydrolysed and worked up as above (compound **20**). Distillation afforded 4.32 g (88%) of pure Pear Ester **22**; b.p. 81–82°/0.1 mmHg (lit.[29] 70–72°/0.05 mmHg); n_D^{20} 1.4881; IR (neat) cm^{-1} 1715 (COOEt), 1640, 1620 (C=C-C=C); ^{1}H NMR (CCl_4, δ) 7.22 (CH=,dd,1), 5.45–5.95 (CH=,m,3), 3.98 (CH_2-O,q,2), 2.13 (CH_2-C=,q,2); ^{13}C NMR ($CDCl_3$, δ) 167.7 (-COO), 141.9, 139.8, 126.8, 121.5 (CH=), 60.4 (CH_2-O), 31.5, 29.2, 28.3, 22.6 (CH_2), 14.3, 14.0 (CH_3). Calc for $C_{12}H_{20}O_2$: C, 73.42; H, 10.26; found: C, 73.41; H, 10.37%.

Alternatively, the same compound may be prepared as follows: 4.9 g (50 mmol) of ethyl propiolate **21** were added, at – 70°, to a stirred solution of cuprate **1** (R = nAm) (25 mmol) in 120 ml Et_2O. The mixture was warmed to room temperature (30 min) then hydrolysed at – 10° with a mixture of 50 ml sat NH_4Cl and 30 ml 20% HCl. After addition of 100 ml hexane and filtration, the organic layer was washed twice with 50 ml of a sat. NH_4Cl solution and dried over $MgSO_4$. Distillation afforded 7.65 g (78%) of **22**.

(Z)-*Methyl-2-carbomethoxy-5-octenoate* **24**. 3.95 g (25 mmol) of dimethyl cyclopropane-1,1-dicarboxylate **23** were added, at – 30°, to a stirred solution of cuprate **1** (R = Et) (25 mmol) in 120 ml Et_2O. The mixture was allowed to warm to – 15° during 15 min and was hydrolysed after 1 hr with a mixture of 50 ml sat NH_4Cl and 30 ml of 10% HCl. Hexane (100 ml) was added, the precipitate was filtered off, and the organic layer was washed once with 50 ml sat. NH_4Cl and dried over $MgSO_4$. Distillation afforded 4.94 g (92%) of pure **24**; b.p. 97–98°/0.2 mmHg; n_D^{20} 1.4450; IR (neat) cm^{-1} 3010 (H-C=C-H), 1760, 1740 (COOMe), 1660 (H-C=C-H) NMR (CCl_4, δ) 5.18 (CH=CH,m,2), 3.57 (O-CH_3,s,6), 3.18 ( $CH\begin{smallmatrix}/COO\\ \backslash COO\end{smallmatrix}$,t,1), 1.88–2.04 (CH_2-,m,6). Calc for $C_{11}H_{18}O_4$: C, 61.66; H, 8.46; found: C, 61.42; H, 8.52%.

(E,Z)-1,1-*Diethoxy-2,4-decadiene* **29**. 3.2 g (25 mmol) of 1,1-diethoxypropyne were added, at – 50°, to an ethereal solution (120 ml) of cuprate **1** (R = nAm) (25 mmol). The solution was warmed to – 25°, kept 2 hr at this temperature, and then was hydrolysed with a mixture of 70 ml sat NH_4Cl solution and 15 ml 17% NH_4OH solution. Hexane (100 ml) was added, the precipitate was filtered off, the organic layer was washed once with 50 ml sat NH_4Cl and dried over $MgSO_4$. Distillation afforded 4.3 g (76%) of pure acetal **29**; b.p. 81–82°/0.01 mmHg; n_D^{20} 1.4619; IR (neat) cm^{-1} 3005, 1660, 1615 (CH=CH), 1130, 1050 {CH(OEt)$_2$}; NMR (CCl$_4$, δ) 6.61 (dd, CH=,1), 6.00 (dd,CH=,1), 5.40–5.70 (CH=, m,2), 4.97 ($\mathrm{CH}<^{\mathrm{O}}_{\mathrm{O}}$,d,1), 3.40–3.60 (O–CH$_2$,m,4), 2.12 (CH$_2$–C=,q,2). Calc for $C_{14}H_{26}O_2$: C, 74.28; H, 11.57; found: C, 74.38; H, 11.62%.

(E,Z)-1-*Phenylthio-2-methyl*-1,3-*hexadiene* **30**. To a stirred solution of cuprate **1** (R = Et) (25 mmol) in Et$_2$O (100 ml) were added 80 ml of THF at −40°. Then 3.7 g (25 mmol) of 1-phenylthio-1-propyne was added and the mixture warmed to 0° (30 min), stirred 1 hr and hydrolysed with a mixture of 60 ml sat NH$_4$Cl and of 20 ml 20% HCl. Hexane (100 ml) was added and, after filtration, the organic layer was washed once with 50 ml 5% NH$_4$OH, then 50 ml of sat NH$_4$Cl and dried over MgSO$_4$. Evaporation of solvents afforded 5.25 g (98%) of product **30** (homogeneous by GLC). Isomerisation occurred during the distillation.

(E)-3-*Octen-2-one* **32**. To a stirred solution of cuprate **1** (R = nBu) (25 mmol) in 100 ml Et$_2$O was added THF (80 ml) at −40°, then 3.5 g (25 mmol) of ethoxyacetylene. The mixture was warmed to −15°, kept 2 hr at this temperature, then hydrolysed with 80 ml of 20% HCl. Hexane (100 ml) was added, the precipitate was filtered off, and the organic layer was washed twice with 50 ml 20% HCl and once with 50 ml sat NH$_4$Cl and finally dried over MgSO$_4$. Distillation afforded 4.73 g (75%) of pure ketone **32**; b.p. 73–74°/14 mmHg (lit.[48] b.p. 100°/50 mmHg); n_D^{20} 1.4518 (lit.[48] n_D^{20} 1.4480); IR (neat) cm^{-1} 1680 (C=O), 1630 (C=C), 985 (H–C=C–H); NMR (CCl$_4$, δ) 6.41 (CH=,dt,1), 5.68 (CH=,d,1), 2.13 (CH$_2$–C=,m,2), 2.02 (CH$_3$,s,3). Calc for $C_8H_{14}O$: C, 76.14; H, 11.18; found: C, 76.01; H, 11.27%.

(E,Z)-1-*Ethylthio*-1,3-*hexadiene* **34**. 50 ml THF were added to a stirred solution of cuprate **1** (R = Et) (12.5 mmol) in 60 ml Et$_2$O, at −40°. Then 2.15 g (25 mmol) of ethylthioacetylene were added and the mixture was warmed to −5° (30 min) stirred 2 hr, and hydrolysed with a mixture of 40 ml sat NH$_4$Cl and 10 ml of 20% HCl. Hexane (60 ml) was added, the precipitate was filtered off, the organic layer was washed successively with 30 ml 3% NH$_4$OH and 30 ml sat NH$_4$Cl and dried over MgSO$_4$. Distillation afforded 3.06 (86%) of compound **34**. b.p. 82–84°/14 mmHg; n_D^{20} 1.5373; IR (neat) cm^{-1} 3010, 1635, 1570 (CH=CH); NMR (CCl$_4$, δ) 6.35 (CH=,dd,1), 6.05 (CH=,d,1), 5.86 (CH=,dd,1), 5.18 (CH=,dt,1), 2.66 (S–CH$_2$,q,2), 2.13 (CH$_2$–C=;m;2). Calc for $C_8H_{14}S$: C, 67.54; H, 9.91; found: C, 67.41; H, 10.02%.

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